

What is claimed is:

1. A self-hardening bioceramic composition, comprising:
2 a hydrated precursor of a calcium phosphate and an aqueous-based liquid
3 in an amount sufficient to hydrate the calcium phosphate to form a paste or
4 putty, characterized in that hardening of the hydrated precursor is associated
5 with an endothermic reaction.
- 6
- 7 2. A self-hardening bioceramic composition, comprising:
8 a hydrated precursor of an amorphous calcium phosphate and an aqueous-
9 based liquid in an amount sufficient to hydrate the calcium phosphate to form a
10 paste or putty, characterized in that hardening of the hydrated precursor occurs
11 in more than ten minutes.
- 12
- 13 3. The composition of claim 2, wherein hardening occurs in more
14 than 30 minutes.
- 15
- 16 4. The composition of claim 1, wherein the aqueous-based fluid is
17 selected from the group consisting of water, a physiologically acceptable pH-
18 buffered solution, saline solution, serum and tissue culture medium.
- 19
- 20 5. The composition of claim 1, wherein the calcium phosphate
21 comprises an amorphous calcium phosphate.
- 22
- 23 6. The composition of claim 1, further comprising a promoter, said
24 promoter capable of promoting the hardening of the hydrated precursor.
- 25
- 26 7. The composition of claim 1, wherein the hardening of the
27 hydrated precursor is further associated with the conversion of the calcium
28 phosphate into a poorly crystalline apatitic calcium phosphate.
- 29
- 30 8. The composition of claim 7, further comprising a promoter, said
31 promoter further capable of promoting the conversion of calcium phosphate into
32 a poorly crystalline apatitic calcium phosphate.

1 9. The composition of claim 6 or 8, wherein the promoter is selected
2 from the group consisting of passive promoters and participant promoters.

3

4 10. The composition of claim 9, wherein the promoter is a passive
5 promoter selected from the group consisting of metals, metal oxides, ceramics,
6 silicates, sugars, salts, and polymeric particulates

7

8 11. The composition of claim 9, wherein the promoter is a passive
9 promoter and said passive promoter is present in the range of about 1:1 to about
10 5:1 calcium phosphate:promoter.

11

12 12. The composition of claim 9, wherein the promoter is a passive
13 promoter selected from the group consisting of SiO_2 , mica, Al_2O_3 , poly(L-lactide)
14 (PLLA), polyglycolide (PGA), and poly(lactide-co-glycolide) (PLGA) copolymers.

15

16 13. The composition of claim 9, wherein the promoter is a participant
17 promoter selected from the group consisting of calcium and phosphorus sources.

18

19 14. The composition of claim 9, wherein the promoter is a participant
20 promoter selected from the group consisting of calcium metaphosphate,
21 dicalcium phosphate dihydrate, heptacalcium decaphosphate, tricalcium
22 phosphates, calcium pyrophosphate dihydrate, crystalline hydroxyapatite, PCA
23 calcium phosphate, calcium pyrophosphate, monetite, octacalcium phosphate,
24 CaO , CaCO_3 , calcium acetate, and H_3PO_4 , and ACP.

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26 15. The composition of claim 9, wherein the promoter comprises
27 DCPD.

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29 16. The composition of claim 9, wherein the promoter comprises
30 DCPD having an average grain size less than about $200\mu\text{m}$.

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1 17. The composition of claim 9, wherein the promoter comprises
2 DCPD having an average grain size of less than about 95 μ m.

3
4 18. The composition of claim 9, wherein the promoter comprises
5 DCPD having an average grain size of about 35 - 45 μ m and a grain size
6 maximum of less than about 110 μ m.

7
8 19. The composition of claim 1, further characterized in that
9 hardening occurs in less than one hour at about 37 °C.

10
11 20. The composition of claim 1, further characterized in that
12 hardening occurs in more than 24 hours at about 4 °C.

13
14 21. The composition of claim 1, wherein the amount of liquid is in
15 the range of about 0.5 to about 2.0 mL liquid/g calcium phosphate.

16
17 22. A bioceramic composition, comprising:
18 a poorly crystalline calcium phosphate prepared by,
19 promoting the hardening of a hydrated precursor comprising an
20 amorphous calcium phosphate and an aqueous-based liquid in an amount
21 sufficient to hydrate the amorphous calcium phosphate to form a paste or putty,
22 whereby hardening is associated with an endothermic reaction and the
23 conversion of the amorphous calcium phosphate into the poorly crystalline
24 calcium phosphate.

25
26 23. A bioceramic composition, comprising:
27 a strongly bioresorbable, poorly crystalline apatitic calcium phosphate.

28
29 24. The composition of claim 22 or 23, wherein said poorly crystalline
30 apatitic calcium phosphate has an X-ray diffraction substantially as shown in
31 Figure 18.

32

1 25. The composition of claim 23, wherein the strongly resorbable,
2 poorly crystalline apatitic calcium phosphate has an X-ray diffraction pattern
3 comprising broad peaks at 2θ values of 26° , 28.5° , 32° and 33° .

4

5 26. The composition of claim 23, wherein the X-ray diffractions
6 pattern is characterized by an absence of peaks associated with the 210 Miller
7 Index.

8

9 27. The composition of claim 23, wherein the poorly crystalline
10 apatitic calcium phosphate is formulated so that when the composite
11 compromises at least 1 g of poorly crystalline apatitic calcium phosphate, at least
12 about 80% of the poorly crystalline apatitic calcium phosphate is resorbed within
13 one year when the composite is placed in a rat intramuscular site.

14

15 28. The composition of claim 23, wherein the poorly crystalline
16 apatitic calcium phosphate is formulated so that when the composite
17 compromises at least 1 g of poorly crystalline apatitic calcium phosphate, at least
18 about 80% of the poorly crystalline apatitic calcium phosphate is resorbed within
19 nine months when the composite is placed in a rat intramuscular site.

20

21 29. The composition of claim 23, wherein the poorly crystalline
22 apatitic calcium phosphate is formulated so that when the composite
23 compromises at least 1 g of poorly crystalline apatitic calcium phosphate, at least
24 about 80% of the poorly crystalline apatitic calcium phosphate is resorbed within
25 six months when the composite is placed in a rat intramuscular site.

26

27 30. The composition of claim 23, wherein the poorly crystalline
28 apatitic calcium phosphate is formulated so that when the composite
29 compromises at least 1 g of poorly crystalline apatitic calcium phosphate, at least
30 about 80% of the poorly crystalline apatitic calcium phosphate is resorbed within
31 three months when the composite is placed in a rat intramuscular site.

32

1 31. The composition of claim 23, wherein the poorly crystalline
2 apatitic calcium phosphate is formulated so that when the composite
3 compromises at least 1 g of poorly crystalline apatitic calcium phosphate, at least
4 about 80% of the poorly crystalline apatitic calcium phosphate is resorbed within
5 one month when the composite is placed in a rat intramuscular site.

6

7 32. The composition of claim 23, wherein the poorly crystalline
8 apatitic calcium phosphate is formulated so that when implanted *in vivo* in a
9 bone site, new bone substantially replaces the composite within six months.

10

11 33. The composition of claim 23, wherein the poorly crystalline
12 apatitic calcium phosphate is formulated so that when implanted *in vivo* in a
13 bone site, new bone substantially replaces the composite within six weeks.

14

15 34. A method of preparing a bioceramic composition, comprising:
16 mixing in any order,
17 (a) an amorphous calcium phosphate,
18 (b) a promoter, and
19 (c) an aqueous-based liquid in an amount sufficient to form a paste or
20 putty, whereby the paste or putty is converted into a poorly crystalline apatitic
21 calcium phosphate and said conversion is associated with hardening of the paste
22 in an endothermic reaction.

23

24 35. The method of claim 34, wherein the promoter is selected from
25 the group consisting of SiO_2 , Al_2O_3 , sand, mica and glass.

26

27 36. The method of claim 34, wherein the promoter is a calcium or a
28 phosphorus source.

29

30 37. The method of claim 34, wherein the calcium phosphate is selected
31 from the group consisting of calcium metaphosphate, dicalcium phosphate
32 dihydrate, heptacalcium decaphosphate, tricalcium phosphates, calcium

1 pyrophosphate dihydrate, crystalline hydroxyapatite, PCA calcium phosphate,
2 calcium pyrophosphate, monetite, octacalcium phosphate, CaO, CaCO₃, calcium
3 acetate, and H₃PO₄, and ACP.

4

5 38. The method of claim 34, wherein the reaction is carried out at no
6 greater than about 37 °C.

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8 39. The method of claim 34, wherein the fluid is selected from the
9 group consisting of water, a physiologically acceptable pH-buffered solution,
10 saline solution, serum and tissue culture medium.

11 *SBR*
12 40. A composite material comprising:
13 (a) a poorly crystalline apatitic calcium phosphate made by the process
14 comprising:

15 providing an amorphous calcium phosphate in the presence of a sufficient
16 quantity of water to produce a paste; and

17 promoting the hardening of the paste, wherein said hardening is associated
18 with the conversion of the amorphous calcium phosphate to a poorly crystalline
19 apatitic calcium phosphate; and

20 (b) a supplemental material in intimate contact with the poorly
21 crystalline apatitic calcium phosphate, said supplemental material present in an
22 amount effective to impart a selected characteristic to the composite.

23

24 41. The material of claim 40 characterized in that, said paste, when
25 prepared from a reaction of amorphous calcium phosphate and a second phosphate
26 in a fluid, the reaction mixture is injectable and formable for a time greater than
27 about 10 minutes at about 25 °C, and hardens within about 10 to 60 minutes at
28 about 37 °C.

29

30 *SBR* 42. A composite material, comprising:
31 a strongly bioresorbable, poorly crystalline apatitic calcium phosphate in
32 intimate contact with a biocompatible supplemental material, said supplemental

1 material present in an amount effective to impart a selected characteristic to the
2 composite.

3

4 43. The composite of claim 42, wherein said poorly crystalline apatitic
5 calcium phosphate has x-ray diffraction substantially as shown in Figure 18.

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7 44. The composite of claim 42, wherein the strongly resorbable, poorly
8 crystalline apatitic calcium phosphate has an X-ray diffraction pattern comprising
9 broad peaks at 2θ values of 26° , 28.5° , 32° and 33° .

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11 45. The composite of claim 42, wherein the poorly crystalline apatitic
12 calcium phosphate is formulated so that when the composite compromises at least
13 1 g of poorly crystalline apatitic calcium phosphate, at least about 80% of the
14 poorly crystalline apatitic calcium phosphate is resorbed within one year when the
15 composite is placed in a rat intramuscular site.

16

17 46. The composite of claim 42, wherein the poorly crystalline apatitic
18 calcium phosphate is formulated so that when the composite compromises at least
19 1 g of poorly crystalline apatitic calcium phosphate, at least about 80% of the
20 poorly crystalline apatitic calcium phosphate is resorbed within nine months when
21 the composite is placed in a rat intramuscular site.

22

23 47. The composite of claim 42, wherein the poorly crystalline apatitic
24 calcium phosphate is formulated so that when the composite compromises at least
25 1 g of poorly crystalline apatitic calcium phosphate, at least about 80% of the
26 poorly crystalline apatitic calcium phosphate is resorbed within six months when
27 the composite is placed in a rat intramuscular site.

28

29 48. The composite of claim 42, wherein the poorly crystalline apatitic
30 calcium phosphate is formulated so that when the composite compromises at least
31 1 g of poorly crystalline apatitic calcium phosphate, at least about 80% of the
32 poorly crystalline apatitic calcium phosphate is resorbed within three months when

1 the composite is placed in a rat intramuscular site.

2

3 49. The composite of claim 42, wherein the poorly crystalline apatitic
4 calcium phosphate is formulated so that when the composite compromises at least
5 1 g of poorly crystalline apatitic calcium phosphate, at least about 80% of the
6 poorly crystalline apatitic calcium phosphate is resorbed within one month when
7 the composite is placed in a rat intramuscular site.

8

9 50. The composite of claim 42, wherein the supplementary material is
10 bioresorbable.

11

12 51. The composite of claim 50, wherein the resorbable supplementary
13 material is selected from the group consisting of collagen, demineralized bone
14 matrix, derivatized hyaluronic acid, polymnydrides, polyorthoesters,
15 polyglycolic acid, polylactic acid, and copolymers thereof, polyesters of α -
16 hydroxycarboxylic acids, poly(L-lactide) (PLLA), poly(D,L-lactide) (PDLLA),
17 polyglycolide (PGA), poly(lactide-co-glycolide) (PLGA), poly(D,L-lactide-co-
18 trimethylene carbonate), and polyhydroxybutyrate (PHB), polyanhydrides,
19 poly(anhydride-co-imide) and co-polymers thereof, and bioactive glass
20 compositions.

21

22 52. The composite of claim 42, wherein supplementary material is non-
23 bioresorbable.

24

25 53. The composite of claim 52, wherein the non-bioresorbable
26 supplementary material is selected from the group consisting of dextrans,
27 polyethylene, polymethylmethacrylate (PMMA), carbon fibers, polyvinyl alcohol
28 (PVA), poly(ethylene terephthalate)polyamide, bioglasses, calcium sulfate and
29 calcium phosphates

30

31 54. The composite of claim 42, wherein the supplementary material is a
32 lubricant.

1 55. The composite of claim 54, wherein the lubricant is selected from
2 the group consisting of silicone oil, polymer waxes, lipids, surfactants and fatty
3 acids.

4

5 56. The composite of claim 42, wherein the supplementary material is
6 in the form selected from the group consisting of foam, sponge, mesh, particles,
7 fibers, gels and filaments.

8

9 57. A method of preparing a ceramic composite material, comprising:
10 mixing in any order,
11 (a) an amorphous calcium phosphate,
12 (b) a promoter, and
13 (c) a supplementary material, the supplementary material present in an
14 amount effective to impart a selected characteristic to the composite; and
15 initiating conversion of the amorphous calcium phosphate into a poorly
16 crystalline apatitic calcium phosphate, said conversion accompanied with hardening
17 at about 37 °C of the composite within 10 to 60 minutes.

18

19 58. The method of claim 57, wherein the promoter is selected from the
20 group consisting of Al_2O_3 , sand, mica and glass.

21

22 59. The method of claim 57, wherein the promoter is a calcium or a
23 phosphorus source.

24

25 60. The method of claim 59, wherein the promoter is selected from the
26 group consisting of calcium metaphosphate, dicalcium phosphate dihydrate,
27 heptacalcium decaphosphate, tricalcium phosphates, calcium pyrophosphate
28 dihydrate, crystalline HA, PCA calcium phosphate, calcium pyrophosphate,
29 monetite, octacalcium phosphate, CaO , CaCO_3 , calcium acetate, and H_3PO_4 , and
30 ACP.

31

32

1 61. The method of claim 57, wherein the reaction is carried out at no
2 greater than about 37 °C.

3

4 62. The method of claim 57, wherein the reaction to form a poorly
5 crystalline apatitic calcium phosphate is initiated before addition of the
6 supplementary material.

7

8 63. The method of claim 57, wherein the reaction to form a poorly
9 crystalline apatitic calcium phosphate is initiated after addition of the
10 supplementary material.

11

12 64. The method of claim 57, wherein the reaction is initiated by
13 addition of a fluid, the fluid selected from the group consisting of water, a
14 physiologically acceptable pH-buffered solution, saline solution, serum and tissue
15 culture medium.

16

17 65. An orthopedic device comprising the composite of claim 42.

18

19 66. A bone cement comprising the composite of claim 42.

20

21 67. A method for embedding an object at a bone site, comprising:
22 preparing a composite comprising a fully resorbable, poorly crystalline
23 apatitic calcium phosphate in intimate contact with a non-resorbable or weakly
24 resorbable supplementary material;

25 introducing the composite to a bone site, whereby the fully resorbable
26 poorly crystalline apatitic calcium phosphate is resorbed and ossified and the non-
27 resorbable supplementary material remains at the bone site.

28

29 68. A method for treating a bone defect, comprising:
30 identifying a bone site suitable for receiving an implant; and
31 introducing a strongly resorbable, poorly crystalline apatitic calcium
32 phosphate at the implant site, whereby bone is formed at the implant site.

1 69. A method for treating a bone defect, comprising:
2 identifying a bone site suitable for receiving an implant; and
3 introducing a hydrated precursor to a strongly resorbable, poorly crystalline
4 apatitic calcium phosphate at the implant site, whereby the hydrated precursor is
5 converted *in vivo* to a poorly crystalline apatitic calcium phosphate and whereby
6 bone is formed at the implant site.

7
8 70. The method of claim 68, wherein the poorly crystalline apatitic
9 calcium phosphate is introduced in the form selected from the group consisting of
10 paste, putty and preshaped object.

11
12 71. The method of claim 69, wherein the hydrated precursor is
13 introduced in the form selected from the group consisting of paste and putty.

14
15 72. The method of claim 70 or 71, characterized in that, said paste is
16 injectable for a time greater than about 10 minutes at about 25 °C, hardens within
17 about 10 to 60 minutes at about 37 °C.

18
19 73. The method of claim 68, wherein said poorly crystalline apatitic
20 calcium phosphate has x-ray diffraction substantially as shown in Figure 18.

21
22 74. The method of claim 68, wherein the strongly bioresorbable, poorly
23 crystalline apatitic calcium phosphate has an X-ray diffraction pattern comprising
24 broad peaks at 2θ values of 26°, 28.5°, 32° and 33°.

25
26 75. The method of claim 68, wherein the strongly bioresorbable, poorly
27 crystalline apatitic calcium phosphate is characterized in that, when placed in a rat
28 intramuscular site, resorption of at least 1 g of the material is at least 80%
29 resorbed within one year.

30
31 76. The method of claim 68, wherein the strongly bioresorbable, poorly
32 crystalline apatitic calcium phosphate is characterized in that, when placed in a rat

1 intramuscular site, resorption of at least 1 g of the material is at least 80%
2 resorbed within one month.

3

4 77. The method of claim 68 or 69, wherein the implant site comprises a
5 tooth socket.

6

7 78. The method of claim 68 or 69, wherein the implant site comprises a
8 non-union bone.

9

10 79. The method of claim 68 or 69, wherein the implant site comprises a
11 bone prosthesis.

12

13 80. The method of claim 68 or 69, wherein the implant site comprises
14 an osteoporotic bone.

15

16 81. The method of claim 68 or 69, wherein the implant site comprises
17 an intervertebral space.

18

19 82. The method of claim 68 or 69, wherein the implant site comprises a
20 alveolar ridge.

21

22 83. The method of claim 68 or 69, wherein the implant site comprises a
23 bone fracture.

24

25 84. A method of preparing a ceramic implant, comprising:

26 mixing in any order,

27 (a) a reactive amorphous calcium phosphate,

28 (b) a second calcium phosphate, the second calcium phosphate and the
29 reactive amorphous calcium phosphate in a proportion to form an apatitic calcium
30 phosphate, and

31 (c) a physiological liquid, said liquid in the amount to provide a paste or
32 putty; and

1 introducing the paste or putty into an implant site.

2

3 85. The method of claim 84, wherein the reaction is carried out at no
4 greater than about 37 °C.

5

6 86. The method of claim 84, wherein the fluid selected from the group
7 consisting of water, a physiologically acceptable pH-buffered solution, saline
8 solution, serum and tissue culture medium.

9

10 87. The method of claim 84, wherein the paste or putty is injected into
11 the implant site.

12

13 88. A method for embedding a prosthetic device into a bone,
14 comprising:

15 introducing an implant device at a bone site;

16 applying a strongly resorbable, poorly crystalline apatitic calcium
17 phosphate in the form of a powder, ~~paste or putty~~ to the implant device,
18 whereby the poorly crystalline apatitic calcium phosphate is resorbed at the
19 implant site and replaced thereby with new bone growth.

20

21 89. A method for treating a bone defect comprising:

22 identifying a bone site suitable for receiving an implant;

23 introducing pressed powder compact at the bone site, said pressed powder
24 compact having approximately the shape required for repair of the bone defect
25 and comprising an amorphous calcium phosphate and a promoter for promoting
26 the conversion of the amorphous calcium phosphate into a strongly resorbable,
27 poorly crystalline apatitic calcium phosphate, whereby the pressed powder
28 compact is converted in vivo into the strongly resorbable poorly crystalline
29 apatitic calcium phosphate.

30